

IN THE CLAIMS:

Please amend the claims, as shown in the Annex to the International Preliminary Examination Report (IPER), as follows:

Please replace claims 1-45 as follows:

1. (Amended) A method for in-vitro testing of active substances in cells comprising at least the following steps:
 - a) providing a cell culture container with an interior chamber and an inside wall and with a first and second membrane system located in the interior chamber, whereby a cell culture space is formed between the first and second membrane systems and the inside wall of the interior chamber;
 - b) providing cells as a cell culture and a cell culture medium in the cell culture space;
 - c) adding a fluid nutrient medium to the cell culture space and removing metabolic products from the cell culture space by means of the first membrane system;
 - d) adding at least one gaseous medium to the cell culture space by means of the second membrane system;
 - e) metering at least one active substance into the cell culture space, with the metering taking place according to an adjusted active substance concentration-time curve; and
 - f) monitoring cell vitality.
2. (Amended) The method according to claim 1, wherein the active substances comprise cytostatics, antibiotics, cytokines, growth factors, or antiviral agents.
3. (Amended) The method according to claim 1, wherein the cell culture comprises primary cells.
4. (Amended) The method according to claim 1, wherein the cell culture comprises tumor cell lines.

5. (Amended) The method according to claim 1, wherein the cell culture space has a minimum volume of at least 0.1 ml and a maximum volume of 5 ml.

6. (Amended) The method according to claim 5, wherein the cell culture space has a minimum volume of 0.3 ml and a maximum volume of 3.0 ml.

7. (Amended) The method according to claim 1, wherein the first membrane system comprises at least one semipermeable membrane or at least one hydrophilic microporous membrane, and the second membrane system comprises at least one gas transfer membrane.

8. (Amended) The method according to claim 1, wherein the first and the second membrane systems comprise hollow fibers stacked in multiple layers.

9. (Amended) The method according to claim 1, wherein the cell culture container comprises a removable lid and the cell culture is provided by adjusting a desired cell density in the cell culture medium, opening the removable lid of the cell culture container, pipetting a desired volume of cell suspension into the cell culture container, and closing the removable lid of the cell culture container so as to close the cell culture container.

10. (Amended) The method according to claim 1, wherein the cell culture medium comprises RPMI 1640.

11. (Amended) The method according to claim 1, wherein the cell culture space comprises at least $1 \cdot 10^5$ cells per ml.

12. (Amended) The method according to claim 1, wherein each cell is at an average distance of 0 μm to 600 μm from the closest membrane in the first and second membrane systems.

13. (Amended) The method according to claim 1, wherein a fluid nutrient medium comprises RPMI 1640.

14. (Amended) The method according to claim 1, wherein the gaseous medium comprises a pO_2 of 0 to 160 mmHg and a pCO_2 of 0 to 115 mmHg.
15. (Amended) The method according to claim 14, wherein the cell culture medium comprises a bicarbonate buffer and the pCO_2 in the gaseous medium is adjusted so that the pH value of the cell culture medium is between 6.8 and 7.8.
16. (Amended) The method according to claim 1, wherein the second membrane system removes gaseous metabolic products from the cell culture space.
17. (Amended) The method according to claim 1, wherein the metering of the at least one active substance comprises adding at least one active substance on a time-staggered basis.
18. (Amended) The method according to claim 1, wherein the metering of the at least one the active substance comprises adding a dose of the at least one active substance to the cell culture space directly or through the first membrane system.
19. (Amended) The method according to claim 1, wherein the active substance concentration-time curve is determined based on permeabilities of the first membrane system, duration of the active substance administration, and active substance concentration.
20. (Amended) The method according to claim 1, wherein the cell culture container is kept at 37°C.
21. (Amended) The method according to claim 1, wherein monitoring of cell vitality comprises measuring the presence of fluorescent dye converted from a cell vitality dye.
22. (Amended) The method according to claim 21, wherein the cell vitality dye comprises Alamar Blue.
23. (Amended) The method according to claim 1, wherein the monitoring of cell vitality comprises at least one sensor.

24. (Amended) The method according to claim 23, wherein the sensor comprises a fluorescence sensor.

25. (Amended) A device for in-vitro testing of active substances in cells, comprising a cell culture container suitable for collecting a cell culture in a cell culture medium with an interior chamber, wherein a first supply device for introducing at least one nutrient medium and a second supply device for adding at least one gaseous medium are located in the interior chamber, wherein each supply device has a supply side and a removal side, and a cell culture space being formed between said supply devices and an inside wall of the interior chamber, and with the first supply device in a fluid connection with the supply side connected to a nutrient medium dispensing unit with at least one nutrient medium container, and the second supply device connected in a fluid connection with the supply side connected to a gas metering unit with at least one gas supply container, wherein the cell culture space has a volume of at most 5 ml and at least 0.1 ml, and further wherein the device comprises an active substance supply container, an active substance dispensing unit, a line system connecting the active substance supply container with the interior chamber for supplying at least one active substance to the cell culture space, and wherein the active substance dispensing unit dispenses the active substance into the cell culture space according to an adjusted active substance concentration-time curve.

26. (Amended) The device according to claim 25, wherein the first supply device includes a fluid connection on the removal side with a waste container.

27. (Amended) The device according to claim 25, wherein the first supply device includes a fluid connection on the removal side by a recirculation line comprising at least one nutrient medium container.

28. (Amended) The device according to claim 25, wherein the first supply device comprises at least one membrane suitable for supplying nutrient media.

29. (Amended) The device according to claim 25, wherein the second supply device comprises at least one membrane suitable for gas exchange.

30. (Amended) The device according to claim 25, wherein the cell culture container comprises a bottom and a lid binding the interior chamber, being opposite one another, and each comprising a transparent material.

31. (Amended) The device according to claim 30, wherein the bottom of the cell culture container includes a heating system.

32. (Amended) The device according to claim 25, wherein the first supply device comprises at least one membrane that is a semipermeable membrane or a hydrophilic microporous membrane.

33. (Amended) The device according to claim 25, wherein the second supply device comprises at least one membrane that is an oxygenation membrane.

34. (Amended) The device according to claim 25, wherein the first and second supply devices comprise membranes that are hollow fibers.

35. (Amended) The device according to claim 34, wherein the hollow fibers are stacked in several layers in the interior chamber.

36. (Amended) The device according to claim 35, wherein the maximum distance between the hollow fibers forming each supply device is between 50 μm and 600 μm .

37. (Amended) The device according to claim 25, wherein the cell culture space comprises a volume of 0.3 ml to 3.0 ml.

38. (Amended) The device according to claim 25, wherein the supply device for adding the active substance comprises at least one active substance supply container, at least one active substance metering device, and a system of lines which connects the at least one active substance supply container through the at least one active substance metering

device directly or through the first supply device with the cell culture space of the cell culture container.

39. (Amended) The device according to claim 25, wherein the device further includes a monitor for cell vitality.

40. (Amended) The device according to claim 39, wherein the monitoring of cell vitality comprises at least one sensor.

41. (Amended) The device according to claim 40, wherein the sensor comprises a fluorescence sensor.

42. (Amended) A modular active substance testing system comprising at least two devices according to claim 25.

43. (Amended) The modular active substance testing system according to claim 42, comprising 6, 24, or 96 devices.

44. (Amended) A process for in-vitro testing of the effects of active substances on cells comprising the device according to claim 25.

45. (Amended) The process according to claim 44, wherein the process comprises determining the influence of pharmacokinetics on cell vitality.

Please add new claim 46 as follows:

--46. A process for in-vitro testing of the effects of active substances on cells comprising the modular active testing substance according to claim 42.--

REMARKS

Claims 1-46 are pending. By this Preliminary Amendment, the specification and claims are conformed to U.S. practice, including adding section headings and addressing antecedent basis issues. Accordingly, no new matter is added by this Preliminary Amendment.